L3 ANSWER 11 OF 31 MEDLINE on STN
AN 2002312092 MEDLINE
DN 22038074 PubMed ID: 12042430
TI The glutamate carboxypeptidase gene II (C>T) polymorphism does not affect **folate** status in the Framingham Offspring cohort.
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NC HL 54776 (NHLBI)
SO JOURNAL OF NUTRITION, (2002 Jun) 132 (6) 1176-9.
Journal code: 0404243. ISSN: 0022-3166.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200206
ED Entered STN: 20020611
Last Updated on STN: 20020626
Entered Medline: 20020625
AB **Glutamate carboxypeptidase II** (**GCPII**) hydrolyzes polyglutamyl folates before their absorption. Recently, a 1561 C>T polymorphism in the **GCPII** gene was reported to be associated with lower **folate** and higher homocysteine plasma concentrations in a small (n = 75) selected elderly population. In this study, we examined the effect of this polymorphism in 680 men and 644 women attending the fifth examination of the Framingham Offspring Study. At the time of sample collection, subjects were not taking any supplements and were not exposed to food **folate** fortification. **GCPII** genotypes were determined by allelic discrimination using Taqman probes. In the population as a whole, this mutation was not associated with lower plasma **folate** level or with elevated plasma homocysteine. In men, plasma **folate** concentrations were higher in carriers of the T allele compared with those homozygotes of the wild-type allele ($P < 0.05$), whereas in women **folate** concentrations did not differ between genotypes ($P = 0.8$). In its relationship to plasma **folate**, this mutation exhibited a weak interaction with age and gender only in older women ($P = 0.05$). Overall, our data show that the **GCPII** C1561T polymorphism is not a determinant of plasma **folate** or total homocysteine concentrations in this large cohort of participants from the Framingham Offspring Study.

L3 ANSWER 7 OF 31 MEDLINE on STN
AN 2003177166 MEDLINE
DN 22581965 PubMed ID: 12694331
TI Genetic determinants of the homocysteine level.
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SO KIDNEY INTERNATIONAL. SUPPLEMENT, (2003 May) (84) S141-4. Ref: 22
Journal code: 7508622. ISSN: 0098-6577.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA English
FS Priority Journals
EM 200307
ED Entered STN: 20030417
Last Updated on STN: 20030717
Entered Medline: 20030716
AB Elevated total homocysteine (tHcy) plasma concentrations indicate **folate** and/or vitamin B12 deficiency and are associated with cardiovascular disease and neural tube defects. Evidence has accumulated that **folate**-, vitamin B12-, and Hcy-metabolism are under genetic control. Because Hcy metabolism is impaired in renal failure, MTHFR 677 C>T, GCP2 1561C>T, RFC1 80G>A, and TCN2 776G>C may further aggravate hyperhomocysteinemia in these patients. The most consistent effect on tHcy plasma concentrations is observed for 677C>T of MTHFR, whereas GCP2, RFC1, and TCN2 polymorphisms show no major effect on tHcy concentrations. Much is yet to be learned about the impact of genetic variants on tHcy levels, human diseases, the genetic-nutrient interactions, as well as the pharmacogenetic consequences in Hcy and vitamin metabolism.

L3 ANSWER 15 OF 31 MEDLINE on STN
AN 2001073218 MEDLINE
DN 20545101 PubMed ID: 11092759
TI **Glutamate carboxypeptidase II**: a polymorphism associated with lower levels of serum **folate** and hyperhomocysteinemia.
AU Devlin A M; Ling E H; Peerson J M; Fernando S; Clarke R; Smith A D; Halsted C H
CS Department of Internal Medicine, University of California, Davis, CA 95616, USA.
NC DK-35747 (NIDDK)
DK-45301 (NIDDK)
SO HUMAN MOLECULAR GENETICS, (2000 Nov 22) 9 (19) 2837-44.
Journal code: 9208958. ISSN: 0964-6906.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AF176574
EM 200101
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010103
AB Low blood **folate** levels result in hyperhomocysteinemia, which has been associated with increased risk for cardiovascular disease, neural tube defects and cognitive deficits. Intake of dietary folates is the chief determinant of blood **folate** levels. Molecular defects in the intestinal absorption of dietary folates that precipitate low blood **folate** levels and hyperhomocysteinemia have not been investigated previously. Dietary folates are a mixture of polyglutamylated folates which are digested to monoglutamyl folates by the action of folylpoly-gamma-glutamate carboxypeptidase (FGCP), an enzyme that is anchored to the intestinal brush border membrane and is expressed by the glutamate carboxypepidase II (**GCPII**) gene. We cloned **GCPII** cDNA from human intestine and identified both a full-length transcript and a 93 bp shorter transcript lacking exon 18, consistent with the presence of a splice variant. In addition, we identified an H475Y polymorphism in **GCPII** in DNA samples from a healthy Caucasian population (n = 75). We found that membranes of transfected COS-7 cells expressing the H475Y variant **GCPII** cDNA had 53% less FGCP activity than did cells expressing wild-type **GCPII**. The presence of the H475Y **GCPII** allele was significantly associated with lower **folate** and higher homocysteine levels in this population. These data suggest that the presence of the H475Y **GCPII** allele impairs the intestinal absorption of dietary folates, resulting in relatively low blood **folate** levels and consequent hyperhomocysteinemia.

L3 ANSWER 22 OF 31 MEDLINE on STN
AN 1999057588 MEDLINE
DN 99057588 PubMed ID: 9838072
TI Mapping, genomic organization and promoter analysis of the human prostate-specific membrane antigen gene.
AU O'Keefe D S; Su S L; Bacich D J; Horiguchi Y; Luo Y; Powell C T; Zandvliet D; Russell P J; Molloy P L; Nowak N J; Shows T B; Mullins C; Vonder Haar R A; Fair W R; Heston W D
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NC DK/CA 47650 (NIDDK)
SO BIOCHIMICA ET BIOPHYSICA ACTA, (1998 Nov 26) 1443 (1-2) 113-27. Journal code: 0217513. ISSN: 0006-3002.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AF007544
EM 199902
ED Entered STN: 19990216
Last Updated on STN: 20000303
Entered Medline: 19990204
AB Prostate-specific membrane antigen (PSMA) is a 100 kDa type II transmembrane protein with **folate** hydrolase and NAALAdase activity. PSMA is highly expressed in prostate cancer and the vasculature of most solid tumors, and is currently the target of a number of diagnostic and therapeutic strategies. PSMA is also expressed in the brain, and is involved in conversion of the major neurotransmitter NAAG (N-acetyl-aspartyl glutamate) to NAA and free glutamate, the levels of which are disrupted in several neurological disorders including multiple sclerosis, amyotrophic lateral sclerosis, Alzheimer's disease and schizophrenia. To facilitate analysis of the role of PSMA in carcinoma we have determined the structural organization of the gene. The gene consists of 19 exons spanning approximately 60 kb of genomic DNA. A 1244 nt portion of the 5' region of the PSMA gene was able to drive the firefly luciferase reporter gene in prostate but not breast-derived cell lines. We have mapped the gene encoding PSMA to 11p11-p12, however a gene homologous, but not identical, to PSMA exists on chromosome 11q14. Analysis of sequence differences between non-coding regions of the two genes suggests duplication and divergence occurred 22 million years ago.

L3 ANSWER 21 OF 31 MEDLINE on STN
AN 1999236452 MEDLINE
DN 99236452 PubMed ID: 10221263
TI Characterization of the enzymatic activity of PSM: comparison with brain NAALADase.
AU Tiffany C W; Lapidus R G; Merion A; Calvin D C; Slusher B S
CS Guilford Pharmaceuticals, Inc., Baltimore, Maryland 21224, USA.
SO PROSTATE, (1999 Apr 1) 39 (1) 28-35.
Journal code: 8101368. ISSN: 0270-4137.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199905
ED Entered STN: 19990607
Last Updated on STN: 20000303
Entered Medline: 19990527
AB BACKGROUND: The prostate cancer marker prostate-specific membrane antigen (PSM) is highly homologous to the brain enzyme N-acetylated alpha-linked acidic dipeptidase (NAALADase). NAALADase is known to cleave terminal carboxy glutamates from both the neuronal peptide N-acetylaspartylglutamate (NAAG) and **folate** polyglutamate. In this report, we compare the NAAG hydrolyzing activity of NAALADase and the prostate enzyme PSM. METHODS: Using a NAAG hydrolytic radioenzymatic assay, we compared the pharmacological and kinetic properties of the brain and prostate enzymes. RESULTS: Eight normal prostate tissues from different species exhibited NAAG hydrolyzing activity. Among 14 cancer cell lines examined, activity was observed in human LNCaP, PC-82, and rat Dunning G and AT-1 cells. Brain exhibited membrane-localized activity exclusively, while the prostate enzyme had activity in both membrane and cytosolic fractions. The only observed pharmacological difference was the sensitivity to their putative substrates, **folate** polyglutamate and NAAG. Kinetically, the soluble form of the prostate enzyme had two catalytic sites, while the membrane-bound form exhibited single site kinetics with a lower Vmax than the brain enzyme, which may suggest a less active hydrolase in the prostate. CONCLUSIONS: The brain enzyme NAALADase and the prostate enzyme PSM are remarkably similar. The importance of the differences in substrate specificities and kinetic parameters remains to be elucidated.